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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WORLEY, CATHY KINGDON	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,308	TAKAIWA ET AL.	
	Examiner	Art Unit	
	CATHY K. WORLEY	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *1-3,11-19,22-25,34-40,42,43 and 46-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10, 20, 21, 26-33, 41, 44, and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Restriction/Election

1. In response to the communication received on Feb. 27, 2008, from Michael L. Goldman, the election with traverse of group II, claims 4-10, 20, 21, 26-33, 41, 44, and 45, is acknowledged.

The Applicant traverses on the grounds that the technical feature linking the inventions is a DNA encoding an allergen-specific T-cell epitope as recited in parts (a), (b), and (c), in claim 1; and the reference relied on by the examiner does not teach such a DNA (see page 8-9 of the response). This is not persuasive, because the claims that were presented for restriction included the original claim 22 which did not require the DNA from claim 1. Furthermore, the seeds claimed in claims 15, 16, 36 and 37 and the cell and breeding material claimed in claims 13, 14, 34, and 35 do not necessarily comprise the DNA, because the parent plant can be heterozygous for the transgene resulting in gametes that do not have the transgene, and therefore ¼ of all seeds produced by self-pollination and 1/2 of all seeds produced by cross-pollination will not comprise the transgene. In addition, even if one were to consider a DNA encoding an allergen-specific T-cell epitope with a storage protein signal sequence or ER-retention sequence under the control of a storage protein promoter; this is obvious over the prior art (see rejection under 35 USC 103). For these reasons, the restriction requirement mailed on Nov. 30, 2007,

is proper and is maintained. The restriction requirement is MADE FINAL. Claims 1-48 are pending in the instant application. Claims 1-3, 11-19, 22-25, 34-40, 42, 43, and 46-48 are withdrawn for being directed to non-elected sequences. Claims 4-10, 20, 21, 26-33, 41, 44, and 45 are examined in this Office Action.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on April 24, 2003. It is noted, however, that applicant has not filed a certified copy of the Japanese application (JP 2003-120639) as required by 35 U.S.C. 119(b). It is also noted that in order to rely on this application to overcome any art rejection, a translation would be required.

Claim Objections

3. Claims 4 and 41 are objected to because of the following informalities: they depend from withdrawn claims of non-elected inventions. Appropriate correction is requested.

4. Claims 9, 10, 20, 30-33, 44, and 45 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s)

to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

- Claims 20, 44, and 45 do not add any limitations to the method from which they depends, therefore, it fails to further limit the parent claim (claims 4, 5, and 6).
- Claims 9, 10, and 30-33 add the limitation that the epitope is accumulated in an edible part of a plant or a seed; and this is and inherent property of using a storage protein promoter; therefore, these claims are redundant over the parent claim because they are merely stating an inherent property of the parent claim.

Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the limitation that the plant into which the DNA is introduced is a rice plant. The current claim includes a method step of introducing the DNA into any plant, but the

preamble is for a rice plant, specifically. Therefore, the starting material for the method must be a rice plant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 4, 5, 7-10, 20, 21, 26, 28, 30, 32, 41, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alli et al (Phytochemistry Reviews (2002) Vol. 1; pp. 55-66) in view of Hirahara et al (J. Allergy Clin. Immunol. (2001) Vol. 108; pp. 94-100).

The claims are directed to a method for accumulating an allergen-specific T-cell epitope in a plant by introducing a DNA comprising a storage protein promoter operably linked to a DNA encoding a storage protein signal sequence and an allergen-specific T-cell epitope or wherein the promoter is operably linked to a DNA encoding a polypeptide in which an allergen-specific T-cell epitope is inserted into a variable region of a storage protein.

Because the recitations of an ER-retention signal are optional (due to "and/or" language), an ER-retention signal is not required. This is a well-known

tool for expression of recombinant proteins, therefore, the Examiner takes official notice that if the claims are amended to require it, adding an ER-retention signal would be obvious over the prior art.

Alli et al teach the production of vaccines for oral delivery of antigens (see entire article). They teach that plant-based edible vaccines may provide an attractive, safe, and inexpensive alternative to convention vaccine production (see abstract). They teach that several different antigens have been successfully produced in plants (see last paragraph on page 56); and they specifically teach the production of a viral glycoprotein in rice seeds using the glutelin (Gt3) promoter and the Gt3 signal peptide (see page 61, Figure 3).

Alli et al do not teach an allergen-specific T-cell epitope.

Hirahara et al teach the production of recombinant peptides that are allergen-specific T-cell epitopes from the Cry j 1 and Cry j 2 proteins from Japanese cedar pollen (see entire article).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the method taught by Alli et al to express the Cry j 1 or Cry j 2 epitopes that are taught by Hirahara et al. One would have been motivated to do so because Alli et al teach that their method can be useful for the production of any edible vaccine and Hirahara et al teach that the Cry j 1 and Cry j 2 peptides were effective for producing positive T-cell responses in more than 90% of the volunteers tested (see page 99). Furthermore, Hirahara et al

teach that peptide based allergen immunotherapy is a new approach to treating allergen-specific T cells, and they teach that Japanese cedar pollinosis is one of the most common seasonal allergic disease in Japan with more than 10% of the population being affected (see page 94) and this demonstrates that there would be a need for immunotherapy directed toward Japanese cedar pollinosis. Given the success of utilizing Cry j 1 and Cry j 2 peptides for immunotherapy that was taught by Hirahara et al and given the successes in producing edible vaccines in plant seeds as taught by Alli et al, one would have had a reasonable expectation of success in producing Cry j 1 and Cry j 2 peptides in rice seeds utilizing the Gt3 promoter and signal peptide.

7. Claims 6, 27, 29, 31, 33, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alli et al (Phytochemistry Reviews (2002) Vol. 1; pp. 55-66) in view of Hirahara et al (J. Allergy Clin. Immunol. (2001) Vol. 108; pp. 94-100) as applied to claims 4, 5, 7-10, 20, 21, 26, 28, 30, 32, 41, and 44 , above, and further in view of Bagga et al (US Patent No. 5,990,384; issued on Nov. 23, 1999) and further in view of Kim et al (Protein Engineering (1990) Vol. 3; pp. 725-731).

The claims are directed to a method for accumulating an allergen-specific T-cell epitope in a plant by introducing a DNA comprising a storage protein promoter operably linked to a DNA encoding a polypeptide in which an allergen-specific T-cell epitope is inserted into a variable region of a storage protein.

Alli et al in view of Hirahara et al teach a method for accumulating an allergen-specific T-cell epitope in a plant by introducing a DNA comprising a storage protein promoter operably linked to a DNA encoding a storage protein signal peptide and an allergen-specific T-cell epitope; as discussed above in the rejection under 35 USC 103 of claims 4, 5, 7-10, 20, 21, 26, 28, 30, 32, 41, and 44.

Alli et al in view of Hirahara et al do not teach a polypeptide in which an epitope is inserted into a variable region of a storage protein.

Bagga et al teach a stable protein that is expressed in a plant as a fusion protein comprising a zein protein (which is a storage protein) and an operably linked protein or peptide (see abstract).

Kim et al teach that modifications of glycinin (which is a storage protein) can be rationally designed by identifying the variable domains and making insertions in the cDNA regions corresponding to variable domains (see abstract).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Alli et al, Hirahara et al, Bagga et al, and Kim et al to arrive at a method of expressing a Cry j epitope as a fusion with a storage protein by inserting the Cry j peptide into a variable region of a storage protein. Bagga et al teach that heterologous proteins, such as antigens, can be expressed in plants transformed with the storage proteins which can act as a carrier protein such that the fusion protein will coalesce and accumulated in the cell as a protein body (see paragraph bridging columns 5 and 6).

Therefore, one would have been motivated to use storage proteins, such as zeins, as carriers for the antigenic cry j peptides. The teachings of Kim et al would have motivated one of ordinary skill in the art to insert the peptide into a variable region of the storage protein. Given the success of utilizing Cry j 1 and Cry j 2 peptides for immunotherapy that was taught by Hirahara et al and given the successes in producing edible vaccines in plant seeds as taught by Alli et al, one would have had a reasonable expectation of success in producing Cry j 1 and Cry j 2 peptides in rice seeds utilizing the Gt3 promoter and signal peptide. Given the success in producing zeins that accumulate to high levels that is taught by Bagga et al and given the success of inserting peptides into the variable regions of a storage protein that is taught by Kim et al, one would have had a reasonable expectation of success in producing fusion proteins comprising Cry j peptides inserted into variable regions of a storage protein.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/
Primary Examiner, Art Unit 1638